201-15208A

Test Plan
for
Diallyldimethylammonium Chloride
(DADMAC)

[CAS No. 7398-69-8]

DADMAC HPV COMMITTEE

c/o RegNet Environmental Services,

1250 Connecticut Avenue, N.W., Suite 700,

Washington, D.C. 20036

Members of the Consortium:

Ciba Specialty Chemicals Corporation.

Nalco Chemical Company

SNF Inc.

Summary

The member companies of the Diallyldimethylammonium Chloride (DADMAC) Panel hereby submit for review and public comment their test plan for DADMAC under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge Program.

DADMAC (CAS No. 7398-69-8) is a monomer used in closed systems in the manufacture of water soluble cationic polymers used as coagulants. There is virtually no exposure to monomer in manufacturing or to polymer during use and the level of monomer in polymer is very low. This product has very low acute and chronic toxicity to experimental animals. There have been no reports of any deleterious effects after several decades of use in industry. DADMAC is not toxic to environmental organisms and is readily biodegradable.

We conclude that there is sufficient data on this intermediate and that no further testing is needed to safeguard human health. However, some testing is proposed to generate additional environmental data which we consider would be valuable.

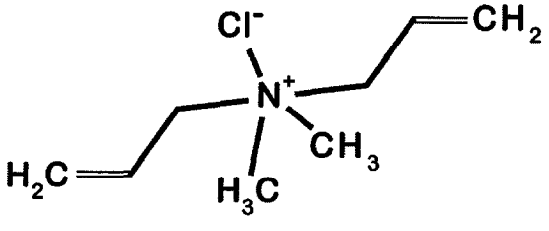
Proposed Test Plan

1. Determination of the acute toxicity in Fathead Minnows (*Pimephales promelas*)
2. Determination of the acute toxicity in *Daphnia magna*
3. Determination of the inhibition in blue-green algae (*Subspicatus capricornutum)*

Identity

Diallyldimethylammonium chloride (DADMAC) is a quartenary ammonium compound which has been has been manufactured in the United States for at least 40 years. It is the reaction product of allylalcohol with dimethylamine. There are currently 3 manufacturing plants for DADMAC monomer in the United States. There is virtually no exposure to monomer during manufacture and emissions to air, water and soil are very low. The product is used almost exclusively as a monomer in the manufacture of cationic, water-soluble polymers which are used in such industries as water-treatment, paper-making and textile printing.

Its structure is shown below:



Diallyldimethylammonium chloride (DADMAC)

Only a small percentage of this monomer enters interstate commerce as most is polymerized on site either as a homopolymer or as a copolymer with acrylamide or other monomers in order to build molecular weight. Best available technology can drive monomer content in polymer down to 1% on an active polymer basis.

Test Data

The test data available on DADMAC is given in the following table:

Environmental Studies
Safety Test in Blue Gill Sunfish
Effect on Soil Organisms
Anaerobic Aquatic Metabolism
Anaerobic Soil Metabolism
Effects of Microbes on Metabolism
Environmental Chemistry Studies
Leachability
Plant Availability
Human Health Studies
Acute Oral Administration in Rats (2)
Primary Skin Irritation (FHSA), Corrosivity (DOT), and Acute Eye Irritation (FHSA)
Segment I Multigeneration Study in Rats
Bacterial Reverse Mutation (Ames) Test (2)
In vitro Mammalian Cell Gene Mutation Test L5178Y TK+/- Mouse Lymphoma
In vitro Mammalian Chromosome Aberration Test in cultured Human Lymphocytes
Oral (Gavage) Rat Teratology
Oral Absorption, Distribution and Excretion Using C14 Labeled Monomer & Polymer
13 Weeks Oral Toxicity Feeding Study in Rats
13 Weeks Oral Toxicity Feeding Study in Dogs

TOXICITY TO AQUATIC ORGANISMS

Tests Conducted on Aquatic Organisms			
Study	**Species**	**Strain**	**Result**
Acute Aquatic Toxicity (72h)	Fish	Blue Gill Sunfish	LC50 = 56 mg/l

The LC50 at 72 hours for Bluegill Sunfish (*Lepomis macrochirus*) is 56 mg/liter (Johnson, 1971). While DADMAC has not been tested in daphnia, other quaternized monomers used for manufacture of cationic polymers, have. The EC50 for daphnia for those substances is greater than 100 mg/liter. ECOSAR structure activity on DADMAC predicts fish, daphnid, and blue-green algae toxicity of 464, 28 and 33 mg/L respectively. An LC 50 in another native species, such as Fathead Minnow (*Pimephales promelas)*, as well as test data for crustaceans, *e.g.*, *Daphnia magna*, and algae *e.g.*, *Subspicatus capricornutum*, would decrease uncertainty in this area. No further testing for health effects is proposed at this time. Evaluation of the acute toxicity of DADMAC to environmental organisms is consistent with the objectives of the EPA HPV Challenge Program.

ENVIRONMENTAL FATE

Environmental Fate Studies	
Study	**Result**
Effect on Soil Organisms	No effect
Anaerobic Aquatic Metabolism	No effect
Effects of Microbes on Metabolism	No effect
Leachability	Mobile
Plant Availability	Low uptake

ACUTE AND CHRONIC TOXICITY

Tests Conducted *In Vivo*			
Study	**Species**	**Strain**	**Result**
Acute Oral Toxicity	Rat	Sprague-Dawley	LD50 = 3030 mg/kg
Primary Skin Irritation	Rabbit	New Zealand White	Not irritating to skin
Corrosivity	Rabbit	New Zealand White	Not corrosive
Acute Eye Irritation	Rabbit	New Zealand White	Not irritating to eyes
Segment I Multigeneration	Rat	Sprague-Dawley	NOAEL = 1.25 mg/kg/day
Oral (Gavage) Teratology	Rat	Sprague-Dawley	NOAEL = 6.0 mg/kg/day
Oral Absorption, Distribution and Excretion	Rat	Not specified	Poorly absorbed
13 Weeks Oral Toxicity Feeding Study	Rat	Not specified	NOAEL = 50.0 mg/kg/day
13 Weeks Oral Toxicity Feeding Study	Dog	Beagle	NOAEL = 200.0 mg/kg/day
Mouse Micronucleus	Mouse	CD1	Negative
Tests Conducted *In Vitro*			
Study	**Species**	**Strain**	**Result**
Ames Test	Bacteria	*Salmonella t.*	Not mutagenic
Ames Test	Bacteria	*Salmonella t.*	Not mutagenic
Chromosome Aberration Test in Cultured Human Lymphocytes			Negative
Mammalian Cell Gene Mutation Test Mouse Lymphoma (L5178Y)			Negative

Acute Toxicity

The acute oral rat LD50 for DADMAC is 3030 mg/kg (Sterner, 1975). DADMAC is non-irritating to rabbit skin and eyes. Since potential human exposure is very low, no further testing is for acute toxicity is proposed.

Mutagenicity

DADMAC has been tested and found negative in the Ames test (San, 1991; de Jouffrey, 1996a), mouse lymphoma (L5178Y) (de Jouffrey, 1996b), and in human lymphocytes for chromosomal aberrations (de Jouffrey, 1996c). DADMAC has also been tested *in vivo* in the mouse micronucleus assay and found negative (Putnam, 1991). There was no mutagenic response in any of these tests. Based on these tests DADMAC is not considered to be mutagenic. No further testing for mutagenicity is proposed.

Repeated Dose Toxicity

DADMAC has been tested in subchronic (13-week) feeding studies in rats and dogs. The NOAEL in rats was 50 mg/kg based on decreased body weight gain in the 500 mg/kg group (LOAEL) (Sterner, 1976). The NOAEL in dogs was 200 mg/kg based on decreased body weight gain in the 800 mg/kg group (Tegeris, 1976). No further subchronic toxicity tests are proposed as the NOAEL is 50 mg/kg. In addition, since DADMAC is clearly non-mutagenic, animal tests for carcinogenicity cannot be justified at this time.

Reproductive and Developmental Toxicity

Teratology and reproduction studies have been performed on the hompopolymer of DADMAC, polyDADMAC. This product contains systematically a significant residual amount of DADMAC monomer. With current, best-available technology, the lowest level of monomeric DADMAC that can be achieved during manufacture of this polymer is 1% by weight on a an active polymer basis. At the time these studies were conducted, the residual DADMAC in polyDADMAC was much higher, probably in the 3 to 5% range.

In the teratology study, there were no effects observed at the highest level of polymer tested, *i.e.*, 600 mg/kg. The animals were exposed to at least 6 mg/kg of DADMAC monomer per day (*i.e.*, 1% of 600 mg/kg/day) (Palmer, 1991). PolyDADMAC was tested

in a Segment I reproduction study (Adamik, 1979). The highest dose tested was 125 mg/kg. No effects were observed at this dose level. The animals were exposed to at least 1.25 mg/kg of DADMAC monomer per day. With a NOAEL in subchronic studies of 50 mg/kg/day and a NOAEL in the teratology study of 6 mg/kg/day, no further studies are proposed for reproductive or developmental toxicity. Furthermore, in the subchronic studies on rats and dogs, no adverse histological findings were reported in the reproductive system of either male or female animals.

Conclusion

No further testing for health effects is necessary.

BACKGROUND INFORMATION: MANUFACTURING & APPLICATIONS

Manufacturing

DADMAC has been manufactured commercially for more than 40 years by the reaction of allyl chloride with dimethyl amine. This is carried out in a closed system since allyl chloride is irritating.

Commercial Application

DADMAC is almost exclusively used in the manufacture of homo- and copolymers (the latter mainly with acrylamide). The concentration of residual monomer in these polymers is between 1 and 5% although current, best-available technology results in the majority of products containing around 1%. These polymers have been extensively tested for toxicity and are non-toxic. They are used in the water-treating, textile printing and paper manufacturing industries.

Shipping and Distribution

Most of the polymers in the US are manufactured at the same site as the monomer is manufactured. Less then 25% of monomer in the US is shipped for polymerization elsewhere.

Worker/Consumer Exposure

There is no significant consumer exposure to DADMAC. Worker exposure is very limited as both monomer and polymer manufacture are carried out in closed systems.

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